REMARKS

The Office Action mailed January 28, 2003, has been received and its contents carefully noted. The pending claims, claims 1-20, were rejected. By this amendment, claims 1-20 have been cancelled and new claims 21-66 are added. The new claims include the limitation that the compound has "an activity that is about 80% or more of its original activity after a period of storage at about 37 °C to about 70 °C". Support may be found in the specification and claims as originally filed. Specific support may be found in the detailed examples and the figures as originally filed. No statutory new matter has been added. Reconsideration and entry of the amendment is respectfully requested.

Claim Objections

The Examiner has objected to claim 19 under 37 C.F.R. 1.75 as being a substantial duplicate of claim 7.

Applicants respectfully submit that claim 19 was not a substantial duplicate of claim 7 as claim 19 further limited the ratio of claim 7. These two ratios are again provided in the new claims presented herein. Reconsideration and withdrawal of the claim objection is respectfully requested.

Rejection under 35 U.S.C. § 102(b)

The Examiner rejected claims 1-10, 15, 19 and 20 under 35 U.S.C. 102(b) as being anticipated by Foster et al. (U.S. Pat. No. 6,258,341). Specifically, the Examiner deemed that Foster et al. disclose a method for producing a dried product which is an amorphous sugar glass without crystals therein which comprises (a) forming an aqueous system which is a solution of (i) one monosaccharide sugar alcohol (mannitol) which would normally form sugar crystals on drying; (ii) a compound which is normally subject to deactivation on drying (Human zinc insulin); and (iii) at least one additive (sodium citrate) which is a glass-former or a formulation-facilitator, the total amount of the additive being sufficient to cause the monosaccharide sugar alcohol to form a glass on drying; wherein the additive itself does not crystallize during the drying step (b); (b) drying the aqueous system at a temperature above its freezing point; and (c) solidifying the component (i), (ii) and (iii) as an amorphous glass without crystals therein,

whereby the amorphous glass stabilizes the compound therein and prevent damage thereto during drying.

Applicants respectfully submit that the new claims as presented herein include the limitation that the compound has "an activity that is about 80% or more of its original activity after a period of time at about 37 °C to about 70 °C". Nowhere do Foster et al. teach or suggest that 80% or more of the activity of the compound, insulin, is retained by the specific sugar glasses disclosed. Foster et al. merely disclose that the percent delivery dose of insulin via inhalation in the exemplified compositions is not significantly affected. Percent delivery dose is not the same as percent activity.

As provided by Foster et al., the percent delivery dose of two compositions may be the same, i.e. same amount of insulin delivered. However, the percent activity of the insulin may be different. Nowhere do Foster et al. disclose the percent activities of the insulin in the compositions. Nowhere do Foster et al. teach or suggest that the activity of insulin may be stabilized. Instead, Foster et al. only disclose that the sugar glasses containing insulin retain the small microparticle formulation such that the delivered dose of insulin is not affected. For inhalable pharmaceuticals, the delivered dose is greatly affected by the particle size of compositions. The particle size affects the dispersibility of an inhalable pharmaceutical. For example, a large particle size will be less dispersible and thereby decrease the delivered dose. Foster et al. only examine the particle sizes, moisture contents, glass transition temperatures, and percent delivered doses over certain storage temperatures and times. Nowhere do Foster et al. examine the percent activity of the insulin after certain storage conditions.

Nowhere do Foster et al. teach or disclose compositions comprising an amorphous sugar glass without crystals therein and at least one compound having an activity that is about 80% or more of its original activity after a period of storage at about 37 °C to about 70 °C. Therefore, Foster et al. do not disclose the present invention as claimed, the rejection under 35 U.S.C. 102(b) should properly be withdrawn.

Rejection under 35 U.S.C. § 103(a)

The Examiner rejected claims 11-14, 16-18 under 35 U.S.C. 103(a) as being unpatentable over Foster et al. Generally, the Examiner deemed that one having ordinary skill in the art would have been motivated, in view of Foster et al., to prepare amorphous glass products of compounds

using different monosaccharide sugar alcohols and/or additives in different percent combinations, depending on cost, availability and/or convenience of use. The Examiner stated that "the preparations of different amorphous glass compositions are well known in the art".

Applicants respectfully agree with the Examiner that various amorphous glass compositions are well known in the art. However, not all amorphous sugar glass compositions stabilize and prevent the activity of certain compounds such as proteins. In fact, as provided by Applicants in the specification of the present invention, many sugars are chemically reactive and cause degradation products. See page 1, second paragraph. Prior to the present invention, some sugars were believed to be good stabilizers and other sugars were believed be poor stabilizers. For example, mannitol was believed to be a poor stabilizer while trehalose was deemed to be a good stabilizer. See page 2, first full paragraph. However, as disclosed in the specification of the present invention, the opposite was unexpectedly found, i.e. mannitol was found to be a good stabilizer and trehalose was found to be a poor stabilizer.

Again, nowhere do Foster et al. teach or suggest that the activity of compounds may be retained or stabilized by amorphous sugar glasses made of monosaccharide sugar alcohols, such as mannitol. Instead, Foster et al. only provide that the delivered dose of insulin may be maintained by sugar glasses. Nowhere do Foster et al. provide assays that show that the activity of insulin is retained after a period of storage under certain conditions. As Foster et al. do not disclose anything about stabilizing the activity of compounds, one of ordinary skill in the art would not be motivated by Foster et al. to make the compositions of the claimed invention in order to stabilize the activity of certain compounds over given periods of time and at temperatures over 37 °C with a reasonable likelihood of success. Therefore, the present invention as claimed is nonobvious and the rejection under 35 U.S.C. 103(a) should properly be withdrawn.

PTO Form 1449

Applicants respectfully resubmit the reference AI that was submitted in an Information Disclosure Statement on December 19, 2000. The Examiner is respectfully requested to initial the PTO Form 1449 to show receipt and consideration of the reference.

Request for Interview

Applicants respectfully request either a telephonic or an in-person interview should there be any remaining issues.

Conclusion

Accordingly, in view of the foregoing amendments and remarks, the Examiner is respectfully requested to reconsider and withdraw the rejection of the claims and to find this application to be in allowable condition.

Respectfully submitted,

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